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Application Number Filing Date		10517509		
		2005-06-13		
First Named Inventor Hen		rman Jan Tijmen Coelingh Bennink et al.		
Art Unit		1614		
Examiner Name Sami		ra Jean-Louis		
Attorney Docket Number		0470-045922		

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	3	5827843		1998-10-27	Koninokx	
	4	5662927		1997-09-02	Ehrlich et al.	
	5	5633242		1997-05-27	Oettel et al.	
	6	5468736		1995-11-21	Hodgen	
	7	5340586		1994-08-23	Pike et al.	
	8	5340585		1994-08-23	Pike et al.	

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9	5340584	1994-08-23	Spicer et al.	
10	5223261	1993-06-29	Nelson et al.	
11	5130137	1992-07-14	Crowley, Jr.	
12	4937238	1990-06-26	Lemon	
13	4762717	1988-08-09	Crowley, Jr.	
14	4722941	1988-02-02	Eckert et al.	
15	4624665	1986-11-25	Nuwayser	
16	4573996	1986-03-04	Kwiatek et al.	
17	4460372	1984-07-17	Campbell et al.	
18	3797494	1974-03-19	Zaffaroni	
19	3440320	1969-04-22	Sackler et al.	

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	1	0185154	wo		A2	2001-11-15	Oregon Heath Scie University et al.	nces		С
	2	1700602	EP		A1	2001-05-18	Pantarhei Bioscieni	ce B.V		
	3	0130357	wo		A	2001-05-03	Theramex			С
	4	0073416	wo		A1	2000-12-07	University of Clincin	nati		С
	5	19917930	DE		A1	2000-10-19	Schering			С
	6	9858657	wo		A1	1998-12-30	Mannaerts et al			С

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7	9603929	wo	A1	1996-02-15	Biex, Inc.	
8	9517895	wo		1995-07-06	Ehrlich et al.	
9	9502408	wo	A1	1995-01-26	Schering	
10	9426207	wo		1994-11-24	University of Southern California	
11	9218107	wo	A1	1992-10-29	University of Southern California	
12	468690	EP	A1	1991-07-17	Sumitomo Chemical Co., Ltd.	
13	0402950	EP	A1	1975-12-18	Orion Yhtymae OY	
14	2426779	DE	A1	1975-12-18	Schering AG	
15	2336434	DE	A1	1975-04-17	Schering AG	
16	2336433	DE	A1	1975-04-03	Schering AG	
17	9603929	wo	A1	1966-02-15		

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T5
	1	VISSER et al., "In vitro effects of estetrol on receptor binding, drug targets and human liver cell metabolism," CLIMACTERIC (2008) 11(1) Appx. II. 1-5.	
	2	VISSER et al., "First human exposure to exogenous single-dose oral estetrol in early postmenopausal women," CLIMACTERIC (2008) 11(1): 1-10.	
	3	VISSER et al., "Clinical applications of esterol," J. Of Steroid Blochem and Molecular Biol. (2009) 114: 85-89.	
	4	HOLINKA et al., "Estebot: A unique steroid in human pregnancy," J. of Steroid Blochem and Molecular Biol. (2009) 110: 138-143.	
	5	COELINGH BENNINK et al., "Oral bioavailability and bone spaning effects of estetrol in an osteoporous model," CLIMACTERIC (2008) 11 (Supp 3): 1-13.	
	6	ALBERTAZZI PACLA et al., "The Effect of Téolone Versus Continuous Combined Novefhisterone Acetate and Cestradoi on Memory, Libido and Mood of Postmeropausal Women: A Pilot study", Database Biosis Online'; 10/31/2000, pages 223-229, Vol. 36, No. 3; Biosciences Information Service, Philadelphia, P.A., U.S.	
	7	ALLEN ET AL., An Overian Homone: Prefirmany Report on Its Localization, Extraction and Partial Purification, and Action in Test Animals, JAMA, September 8, 1923, Vol. 81, pp. 819-821.	
	8	ALLEN ET AL., The Induction of a Sexually Mature Condition in Immature Females by Injection of the Ovarian Folicular Hormone, Am. J. Physiol., 1924, Vol. 69, pp. 577-588.	
	9	JONES ET AL., The Effects of Various Steroids on the Vaginal Histology in the Rat, Fertility and Sterility, April 1973, Vol. 24, No. 4, pp. 284-291.	

NON-PATENT LITERATURE DOCUMENTS

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	Application Number		10517509	
	Filing Date		2005-06-13	
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	Art Unit		1614	
	Examiner Name	Sami	ra Jean-Louis	
	Attorney Docket Number		0470-045922	

10	TULCHINSKY ET Al, Plasma Esterol as an Index of Fetal Well-Being, J. Clin. Endrocrinol. Metab., 1975, Vol 40, Pp. 560-567.	
11	JOZAN ET AL., Different Effects of Cestradiol, Cestriol, Cestrol and of Cestrone on Human Breast Cancer Cells (MCF-7) in Long Term Tissue Culture, Acta Endocrinologica, 1991, Vol. 98, pp. 73-80.	
12	HAMMOND ET AL., A Versatile Method for the Determination of Serum Cortsol Binding Globulin and Sex Hormone Binding Globulin Binding Capacities, 1983, Vol. 132, pp. 101-110.	
13	ELGER ET AL., Sulfamates of Various Estrogens are Prodrugs with increased Systemic and Reduced Hepatic Estrogenicity at Oral Application, J. Steroid Biochem. Molec. Biol., 1995, Vol. 55, No. 374, pp. 395-403.	
14	MURPHY ET AL., Endometrial Effects of Long-Term Low-Dose Administration of RU486, Fertility and Sterility, April 1995, Vol. 63, No. 4, pp. 761-786.	
15	REEL ET AL., Survey and Assessment of Mammalian Estrogen Biological Assays for Hazard Characterization, Fundamental and Applied Toxicology, 1996, Vol. 34, pp. 288-305.	
16	BERAL ET AL., Use of HRT and the Subsequent Risk of Cancer, Journal of Epidemiology and Biostatistics, 1999, Vol. 4, No. 3, pp. 191-215.	
17	TAVANI ET AL., The Adverse Effects of Hormone Replacement Therspy, Drugs & Aging, May 1999, Vol. 14, No. 5, pp. 347-357.	
18	PIKE ET AL., Progestins and Menopause: Epidemiological Studies of Risks of Endometrial and Breast Cancer, Steroids, 2000, Vol. 65, pp. 359-664.	
19	AVVAKUMOV ET AL., Steroid-binding Specificity of Human Sex Hormon-binding Globulin is influenced by Occupancy of a Zinc-binding Site, The Journal of Biological Chemistry, August 25, 2000, Vol. 275, No. 34, pp 25920-25925	
20	HOLINKA ET AL., "In Vivo Effects of Esterol on the Immature Rat Ulerus", Biology of Reproduction, Society for the Reproduction Society for the Study of Reproduction, Champaign, IL, US, March 1979 (1979-05), Vol. 20, No. 2, pp. 242-246.	

Application Number		10517509			
Filing Date		2005-06-13			
First Named Inventor		Herman Jan Tijmen Coelingh Bennink et al.			
Art Unit		1614			
Examiner Name Sami		a Jean-Louis			
Attorney Docket Number		0470-045922			

21	HOLINKA, ET AL., "Comparison of Effects of Esterol and Tamostfen with Those of Estrol and Estradic on the Immature Rat Uterus," Biology of Reproduction, society for the Reproduction Society for the Study of Reproduction, Champargn, IL, US, 1980, Vol. 22, No. 4, pp. 913-926.	
22	JANSSON ET AL, "Estrogen induces a Potent Suppression of Experimental Autoimmune Encephatomyelitis and Collagen-Induced Arthritis in Mice", Journal of Neuroimmunology, Elsevier Science Publishers BV XX, 1994, Vol. 53, No. 2, pp. 203-207.	
23	ERDBRUEGGER ET AL., Drug Discovery Today: Disease Mechanisms (2004), Vol. 1, pg. 73-81.	
24	Lab Tests Online (www.labtestsonline.org/understanding/conditions/autoimmune.html) retrieved on 10/15/2009.	
25	www.liscali.co.uk/lifestyle/health/fitness/health_adviosihetoidor/archive000489.html, retrieved on10/15/2009.	
26	Mediline/Tipus Medical Encyclopedus Malgiae Scienceia, retrieved on 03/28/2008 via www.nitm.nih.gov/imedineplus/ency/ willca00/0777.htm, dateo on 05/06/2007, Paga 1 and 2, also see WebMD: Multiple Scienceia - Prevention, retrieved on 03/28/2008 via www.webmc.com/impliges-dereosia/fundlingle-scienceia-fung-prevention, called on 03/28/2008.	
27	MedinePlus Medical Encyclopedia: rheumatoid arthrifis, retrieved on 03/28/2008 via www.nim.nih.gov/imedineplus/ ency/article/200431 htm, dated on 07/27/2007, page 1-2 and 4; also WebMD: Rheumatoid Arthrifis - Prevention, retrieved on 03/28/2008 via www.webmd.com/irheumatoid-arthrifis/for/theumatoid-arthrifis-prevention, dated on 08/23/2006.	
28	TSENG et al., "Heterogeneity of Saturable Estradiol Binding Sites in Nuclei of Human Endometrum. Estetrol Studies", (1978), Vol. 9, pp 1145-1148.	
29	FISHMAN et al., "Fate of 15 or-Hydroxyestriol-3H in Adult Man", J. Clin. Endocrinol. Metab., (1970), Vol. 31, pp 436.438	
30	LEVINE et al., "Uterine vascular effects of esletrol in nonprognant ewes", Am. J. Obslet. Gynecol., (1994), [148], Vol. 73, pp 735-738.	
31	MARTUCCI et al., "Direction of Estradiol Metabolish as a Control of its Hormonal Action - Uterotrophic Activity of Estradiol Metabolites", Endocrin., (1977), Vol. 101, pp 1709-1715.	

Application Number		10517509		
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Art Unit		1614		
Examiner Name Sa		amira Jean-Louis		
Attorney Docket Numb	er	0470-045922		

32	MARTUCCI et al., "Ulterine Estrogen Receptor Binding of Catecholestrogens and of Estetrol (1,3,5(10)-Estratmene-3, 15a, 16a, 17 (6-Tetrolly, Steroids, (1976), Vol. 27, pp 325-333.	
33	SEEGER et al., 'The inhibitory effect of endogenous estrogen metabolies on copper-mediated in vitro oxidation of LDL', Int. Journal of Clinical Pharmacology and Therapeutics, (1998), Vol. 36, No. 7, pp 383-385.	
34	TSENG et at, "Competition of Estetrol and Ethymylestration with Estration for Nuclear Binding in Human Endometirum", Journal of Steroid Biochemistry, (1976), Vol. 7, pp 817-822.	
35	KUIPERS ET AL., "Enterohepatic Circulation in the Rai", Gastroenterol., Vol. 88, pp 403-411 (1985).	
36	SCHWARTZ, "A Model for the Regulation of Ovulation in the Rait", Recent Prog. Horm. Res., Vol. 25, pp 1-55, (1989).	
37	BEATTIE ET AL, "The Differential Effects of Diestrous Progestogen Administration on Proestrous Gonadotrophin Levels, Endocrinol", Vol 97, pp. 885-890, (1975).	
38	DE VISSER ET AL., "Endocrinological Studies with (7a, 17 a)-17-Hydroxy-7-me norpregn-5(10)-en-20-yn-3-one (Org OD 14), Arznerm, Forsh., Vol. 34, pp 1010-1020, (1984).	
39	National Cancer Institute: Breast cancer prevention retrieved online 08/07/2007 from the internet; http://www.cancer. gov/templotes/doc.aspx?viewed+D972A748-025A-4F65-88ED-33EB3C0450E48version, page 1.	
40	Medine Plus Medical Encyclopedia: Ovarian cancer retrieved online on 08/09/2007 from the internet. https://www.nlm. nh.gov/medineplus/ovariancancer.html, page 1 dated 07/31/2007.	
41	COELINGH-BENNINK ET AL., "Estetrol review: profile and potential clinical applications", International Menopause Society, CLIMATERIC, Vol. 11, (Suppl 1), pp. 47-58 (2008).	
42	SPEROFF ET AL., Clinical Gynecologic Endocrinology and Infertility, Seventh Edition, page 270 (partial).	

	Application Number		10517509	
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	Attorney Docket Numb	er	0470-045922	

		43	WHITE ET AL., "The pharmacokinetics of Intravenous Estradiot: A Preliminary Study", Pharmacotherapy, Vol. 18, pp. 1343-1346, (1998) (Abstract).		
44 HAMMOND ET AL. "Esterol does not bind sex hormone binding globulin or increase its production by human cells", International Menopause Society, CLIMATERIC, Vol. 11, (Suppl. 1), pp. 41-45, (2005).		HAMMOND ET AL., "Estetrol does not bind sex hormone binding globulin or increase its production by human HepG2 cells", international Memopause Society, CLIMATERIC, Vol., 11, (Suppl. 1), pp. 41-46, (2008).			
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